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Original Paper

Association of the Zhejiang University Index with Sleep-related Problems in US Adults: Findings from NHANES 2007-2014

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Abstract

Background: *This study aims to investigate the precise relationship between the Zhejiang University index (ZJU index) and sleep-related problems.*

Methods: *This study included 7920 participants from the National Health and Nutrition Examination Surveys conducted between 2007 and 2014. Logistic regression, restricted cubic spline regression, subgroup analyses and receiver operating characteristic (ROC) curve were employed to evaluate the relationship between the ZJU index and sleep-related problems.*

Results: *After adjusting for all included confounders, the odds ratios (ORs) for sleep disorders, self-reported difficulty falling asleep, and short sleep duration were 1.83 (95%CI: 1.55 to 2.15, P < 0.001), 1.24 (95%CI: 1.12 to 1.37, P < 0.001), 1.17 (95%CI: 1.08 to 1.27, P < 0.001), respectively. A U-shaped nonlinear relationship between the ZJU index and sleep disorders (P-nonlinear = 0.001, point= 37.7) was identified through restricted cubic spline analysis. ROC curve analysis revealed that the ZJU index was superior to single indicators and lipid metabolism indicators in predicting sleep-related problems. Furthermore, it had a high predictive value (area under the curve = 0.710) in elderly women whose sleep disorders were diagnosed.*

Conclusion: *The ZJU index is strongly associated with sleep-related problems in US adults. Therefore, focusing on high ZJU index levels is useful for early monitoring of sleep-related problems, especially in elderly women.*

Keywords

ZJU index, Sleep disorders, Difficulty falling asleep, NHANES, Glucose metabolism, Lipid metabolism

1. Introduction

Sleep-related problems, including difficulty falling asleep, insufficient sleep duration, and sleep disorders, are common diseases that severely affect population health and quality of life [1]. A prior study indicated that about 83.6 million US adults sleep less than seven hours per day [2]. Additionally, individuals with sleep disorders incur healthcare costs ranging from $3,400 to $5,200 per person, which is significantly higher compared to those without sleep problems [3]. It is widely confirmed that sufficient sleep duration, satisfactory sleep quality, and appropriate duration of falling asleep are components of healthy sleep [4]. Good sleep habits contribute to the balance of circadian rhythm. The study showed that the disorders of circadian rhythm could impair metabolism and contribute to the pathogenesis of metabolic diseases [5]. Neuroendocrine activity, which is a major mediator of systemic metabolism, could be easily altered by sleep-related problems [6]. Therefore, sleep-related problems, especially short sleep duration (< 7 hours per night), are often accompanied by disorders in the body's metabolic levels such as insulin resistance, metabolic abnormalities, and weight gain [7]. Kelly et al. illustrated that increased social jet lag in patients with type 2 diabetes is associated with poorer blood sugar control [8]. Schipper et al. strongly advocated for the proactive assessment of potential sleep disorders as a more effective preventive measure against the onset of type 2 diabetes [9]. Concurrently, reduced sleep duration is linked to increased visceral fat, which in turn contributes to diminished sleep quality [10]. The accumulation of visceral fat leads to a decrease in sleep quality. It can be inferred that sleep quality can be improved by controlling weight and improving metabolic capability [11].

The Zhejiang University index (ZJU index), which is a new and comprehensive metabolic indicator, is a powerful identification index for non-alcoholic fatty liver disease (NAFLD) in Chinese population, including the measuring of triglycerides (TG), fasting plasma glucose (FPG) and body mass index (BMI) [12]. Cohort study has shown that the ZJU index has a strong predictive ability to identify NAFLD in overweight women in Western countries [13]. WANG et al. demonstrated the ZJU index was significantly correlated with obstructive sleep apnea syndrome in the middle-aged and elderly population in China [14]. The predictive ability of the ZJU index for sleep-related problems is worth exploring.

This article aims to explore the relationship between the ZJU index and sleep-related problems and explore if the ZJU index could be an effective screening tool for sleep-related problems.

2. Materials and Methods

2.1 Study Design

This study utilized data sourced from the National Health and Nutrition Examination Survey (NHANES) spanning the years 2007 to 2014. The initial estimated sample size was 40,617. Participants were included based on the following specific criteria: (1) minors (age < 18 years), (2) participants with incomplete data for calculating the ZJU index, (3) participants with missing data on sleep-related problems, (4) participants with missing covariate data, and (5) participants with missing weight coefficients. Finally, a total number of 7920 individuals satisfied the inclusion requirements and were incorporated into this study (Figure 1). Following ethical approval, informed consent was obtained from each participant in the NHANES study [15,16]. The National Center for Health Statistics provides detailed information regarding ethical approval procedures and informed consent policies.

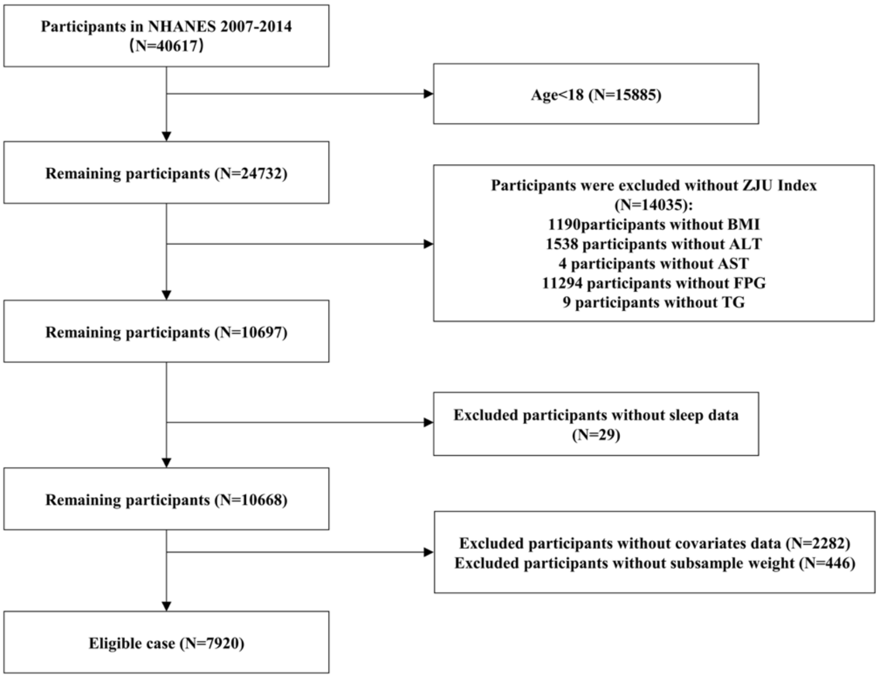

Figure 1. Flowchart of the Sample Selection from NHANES 2007–2014

Note. ALT: alanine aminotransferase; AST: aspartate aminotransferase; BMI: body mass index; FPG: fasting plasma glucose; NHANES: National Health and Nutrition Examination Survey; TG: triglycerides; ZJU index: Zhejiang University index.

2.2 Definition of the ZJU Index

The ZJU index was calculated as body mass index (kg/m^2) + 3*alanine aminotransferase (ALT) (U/L)/aspartate aminotransferase (AST) (U/L) + FPG (mmol/L) + ratio (+ 2 for females) + TG (mmol/L) [17]. In this study, AST, ALT, TG, BMI, and FPG were derived from laboratory and body measurement data, with the ZJU index as a continuous variable.

2.3 Definition of Sleep-related Problems

Sleep duration was calculated based on the answers to SLD010H in the sleep disorders questionnaire (SLQ). The recorded sleep durations were classified into three categories: long sleep duration (> 9 hours per night), normal sleep duration (7-9 hours per night), and short sleep duration (< 7 hours per night) [18]. The SLQ050 question of the SLQ was used to assess self-reported difficulty falling asleep, while the SLQ060 referred to assess sleep disorders [19]. Any short sleep duration, long sleep duration, self-reported difficulty falling asleep, or sleep disorders were defined as the presence of sleep-related problems ("Yes" or "No"), while “don’t know” and “refuse” responses were considered missing. The details of the questionnaire are presented in the supplementary materials.

2.4 Evaluation of Covariates

Covariates considered in this study included factors that may influence sleep-related problems, as well as variables commonly used in many studies. Demographic variables included age, race, marital status, education, and poverty-income ratio (PIR). The laboratory variable included glycosylated hemoglobin (HbA1c). In addition, factors obtained from the questionnaire included smoking status, alcohol consumption, work activity patterns, physical activity patterns, hypertension, hyperlipidemia, depression, and the presence of cardiovascular disease (CVD). Individuals with a score more than 9 on the Patient Health Questionnaire-9 (PHQ-9) were defined as depression. PHQ-9 is a nine-item screening instrument that asked questions regarding the frequency of symptoms of depression over the past two weeks [20]. Both questionnaire responses and laboratory data were employed to evaluate the presence of hypertension and hyperlipidemia. Individuals were classified as having CVD if they had been diagnosed with myocardial infarction, heart failure, coronary heart disease, or stroke.

2.5 Statistical Analysis

The sample weights of the NHANES 2007-2014 fasting subsample were used to obtain nationally representative estimates for all analyses. Simultaneously, considering the stratification and clustering effects caused by the complex sample design, the weight adjustment method involved multiplying the survey weights from 2007 to 2014 by a factor of 1/4. Categorical variables were expressed as counts and their corresponding weighted proportions (%), and associations were assessed using χ^2 tests; Continuous data were compared using the t-tests. Continuous variables that did not follow normal distribution were expressed using median and interquartile range (IQR).

Logistic regression models were used to investigate the relationship between the ZJU index (per 10-point increase) and sleep-related problems. In the multivariate logistic regression models, the ZJU index was treated as a continuous variable. Model 1 was unadjusted for covariates. Model 2 was adjusted for demographic factors such as age, HbA1c, race, education level, marital status, and PIR. Model 3 was adjusted for all variables. To better explore the distribution of the ZJU index and sleep-related problems in the population, the ZJU index was divided into four categories: Q1 (23.31 to 34.71), Q2 (34.70 to 39.19), Q3 (39.19 to 44.67), and Q4 (44.67 to 97.20), based on the distribution of sampled populations.

A smoothing curve fitting was used to investigate the nonlinear relationship between the ZJU index and sleep-related problems among subgroups of US adults, which was described by restricted cubic spline (RCS) regression and threshold effect analysis. The Akaike Information Criterion was employed within the RCS model to determine the optimal number and placement of knots, thereby ensuring an ideal fit and preventing overfitting. Three nodes exhibiting significant differences were chosen for the synthesis of the RCS curve. The fitted models produced adjusted odds ratios. The inflection point's location, along with the trend changes before and after it, were determined through threshold effect analysis.

In addition, subgroup analysis was performed to explore whether the ZJU index has potential differences in sleep-related problems among different populations. The final analysis sample was stratified by the previously mentioned covariates.

Since the ZJU index includes TG, the receiver operating characteristic (ROC) curve and the area under the curve (AUC) were used to evaluate the superiority of the ZJU index over single indicators and lipid metabolism indicators such as high-density lipoprotein (HDL) and total cholesterol (TC).

Data analysis was executed using R software version 4.4.2. Statistical significance was determined by a two-sided test with a p-value less than 0.05.

3. Results

3.1 Baseline Data of Study Participants

The screening process of the data is shown in Figure 1. Due to missing information on any covariates, 40,617 participants were excluded, and the final sample included 7,920 participants. Table 1 presents participants' characteristics classified by sleep-related problems. Among them, the median and IQR of the ZJU index was 38.74(34.41, 44.18), the ZJU index of the people without sleep-related problems was 38.37(34.16, 43.65), and the ZJU index of the people with sleep-related problems was 39.36(35.06, 45.28).

Table 1. Weighted Baseline Characteristics of Participants

Characteristic	**Overall** N = 7920	**No sleep-related problems** N =4645	**Sleep-related problems** N = 3275	***P*-value**
ZJU index, median (IQR)	38.74(34.41, 44.18)	38.37(34.16, 43.65)	39.36(35.06, 45.28)	< 0.001
Gender, N (%)				0.029
Female	4028 (51%)	2385 (52%)	1643 (49%)	
Male	3892 (49%)	2260 (48%)	1632 (51%)	
Age level, N (%)				< 0.001
< 35	1979 (28%)	1200 (28%)	779 (28%)	
35-64	4077 (54%)	2260 (53%)	1817 (57%)	
≥ 65	1864 (18%)	1185 (19%)	679 (15%)	
Race, N (%)				< 0.001
Mexican American	1171 (7.9%)	715 (7.9%)	456 (7.9%)	
Non-Hispanic Black	1474 (11%)	664 (7.5%)	810 (16%)	
Non-Hispanic White	3790 (70%)	2417 (74%)	1373 (63%)	
Other Hispanic	762 (4.9%)	426 (4.5%)	336 (5.7%)	
Other Race	723 (6.3%)	423 (5.8%)	300 (7.2%)	
Education, N (%)				0.002
Over high school	717 (4.8%)	413 (4.5%)	304 (5.2%)	
Completed high school	1181 (12%)	651 (11%)	530 (14%)	

Below high school	6022 (83%)	3581 (85%)	2441 (81%)	
Marital, N (%)				< 0.001
Married/Living with partner	4800 (64%)	2882 (66%)	1918 (61%)	
Widowed/Divorced/Separated	1724 (18%)	944 (16%)	780 (20%)	
Never married	1396 (18%)	819 (18%)	577 (19%)	
PIR, N (%)				< 0.001
High income	2458 (42%)	1559 (46%)	899 (36%)	
Middle income	2932 (36%)	1713 (35%)	1219 (38%)	
Low income	2530 (22%)	1373 (20%)	1157 (26%)	
BMI, median (IQR)	27.70 (24.07, 32.17)	27.40 (23.93, 31.70)	28.35 (24.50, 33.00)	< 0.001
FPG, median (IQR)	99.00 (92.00, 107.00)	99.00 (92.00, 107.00)	99.00 (92.00, 108.00)	0.023
ALT, median (IQR)	21.00 (17.00, 28.00)	21.00 (17.00, 28.00)	21.00 (17.00, 29.00)	0.109
AST, median (IQR)	23.00 (19.00, 27.00)	23.00 (19.00, 27.00)	22.00 (19.00, 28.00)	0.405
TG, median (IQR)	103.00 (73.00, 152.00)	103.00 (72.00, 151.00)	105.00 (75.00, 153.00)	0.211
HbA1c, median (IQR)	5.40 (5.20, 5.70)	5.40 (5.20, 5.70)	5.50 (5.20, 5.80)	0.002
Smoke, N (%)				< 0.001
Never	4366 (56%)	2636 (58%)	1730 (52%)	
Former	1965 (25%)	1229 (26%)	736 (23%)	
Now	1589 (20%)	780 (16%)	809 (25%)	
Drink, N (%)				< 0.001
Never	1050 (11%)	626 (11%)	424 (11%)	
Former	1421 (15%)	781 (13%)	640 (17%)	
Mild	2665 (37%)	1634 (38%)	1031 (34%)	
Moderate	1165 (17%)	691 (18%)	474 (15%)	
Heavy	1619 (21%)	913 (20%)	706 (23%)	
Work Activity, N (%)				< 0.001
No	4664 (56%)	2824 (58%)	1840 (53%)	
Moderate	1774 (24%)	1032 (24%)	742 (23%)	
Vigorous	313 (4.0%)	167 (3.8%)	146 (4.5%)	
Moderate and vigorous	1169 (16%)	622 (14%)	547 (19%)	
Physical Activity, N (%)				< 0.001
No	4063 (46%)	2258 (44%)	1805 (51%)	
Moderate	2177 (29%)	1342 (30%)	835 (27%)	
Vigorous	626 (9.0%)	388 (9.3%)	238 (8.4%)	
Moderate and vigorous	1054 (16%)	657 (17%)	397 (14%)	
Hypertension, N (%)				< 0.001

No	4596 (62%)	2820 (65%)	1776 (58%)	
Yes	3324 (38%)	1825 (35%)	1499 (42%)	
Hyperlipidemia, N (%)				0.488
No	2133 (28%)	1224 (28%)	909 (28%)	
Yes	5787 (72%)	3421 (72%)	2366 (72%)	
CVD, N (%)				0.089
No	7058 (91%)	4176 (92%)	2882 (90%)	
Yes	862 (9%)	469 (8.5%)	393 (9.8%)	
Depression, N (%)				< 0.001
No	7226 (92%)	4365 (95%)	2861 (89%)	
Yes	694 (7.5%)	280 (5.3%)	414 (11%)	

Note. ALT: alanine aminotransferase; AST: aspartate aminotransferase; BMI: body mass index; CVD: Cardiovascular disease; FPG: fasting plasma glucose; HbA1c: glycosylated hemoglobin; PIR: poverty income ratio; TG: triglycerides; ZJU index: Zhejiang University index.

The continuous variables were shown as weighted median and interquartile range. The categorical variables were shown as weighted number with weighted proportion.

All estimates were weighted to be nationally representative.

3.2 Association between the ZJU Index and Sleep-related Problems

In Model 1, the OR for sleep disorders was 1.95 (95%CI: 1.73 to 2.21, $P < 0.001$), while for self-reported difficulty falling asleep and short sleep duration, the ORs were 1.33 (95%CI: 1.22 to 1.45, $P < 0.001$) and 1.23 (95%CI: 1.13 to 1.32, $P < 0.001$), respectively. After adjusting for demographic variables and HbA1c in Model 2, a 10-point increase in the ZJU index is associated with an OR of 1.94 for sleep disorders (95%CI: 1.68 to 2.25, $P < 0.001$), an OR of 1.32 for self-reported difficulty falling asleep (95%CI: 1.19 to 1.46, $P < 0.001$), and an OR of 1.20 for short sleep duration (95%CI: 1.10 to 1.30, $P < 0.001$). In Model 3, the ORs for sleep disorders, self-reported difficulty falling asleep, and short sleep duration were 1.83 (95%CI: 1.55 to 2.15, $P < 0.001$), 1.24 (95%CI: 1.12 to 1.37, $P < 0.001$), 1.17 (95%CI: 1.27 to 1.30, $P < 0.001$), respectively. The ORs of long sleep duration was not statistically significant ($P \geq 0.05$).

In the *P* for trend, the ZJU index was treated as a categorical variable (quartiles) after adjusting for all confounders. The association between the highest quartile (Q4) and sleep-related problems remained strong when compared to the lowest quartile (Q1). Specifically, the OR for sleep disorders was 3.10 (95%CI: 2.05 to 4.68, $P < 0.001$), the OR for self-reported difficulty falling asleep was 1.40 (95%CI: 1.11 to 1.96, $P = 0.005$), and for short sleep duration was 1.51 (95%CI: 1.25 to 1.83, $P < 0.001$) in Model 3. All results above are shown in Table 2.

Table 2. Association of the ZJU Index with Sleep-related Problems

	Characteristic (Per 10 points increase)	Model 1 (OR, 95% CI)	*P*-value	Model 2 (OR, 95% CI)	*P*-value	Model 3 (OR, 95% CI)	*P*-value
Sleep disorders	ZJU (continuity)	1.95 (1.73, 2.21)	< 0.001	1.94 (1.68, 2.25)	< 0.001	1.83 (1.55, 2.15)	< 0.001
	ZJU (continuity)						
	Q1	Reference		Reference		Reference	
	Q2	1.15 (0.80, 1.66)	0.4	1.05 (0.73, 1.52)	0.8	1.04 (0.70, 1.54)	0.8
	Q3	1.83 (1.30, 2.58)	< 0.001	1.67 (1.17, 2.39)	0.006	1.57 (1.05, 2.35)	0.029
	Q4	4.07 (2.93, 5.64)	< 0.001	3.63 (2.53, 5.20)	< 0.001	3.10 (2.05, 4.68)	< 0.001
Self-reported difficulty falling asleep	ZJU (continuity)	1.33 (1.22, 1.45)	< 0.001	1.32 (1.19, 1.46)	< 0.001	1.24 (1.12, 1.37)	< 0.001
	ZJU (categorical)						
	Q1	Reference		Reference		Reference	
	Q2	1.20 (1.00, 1.43)	0.045	1.12 (0.94, 1.33)	0.2	1.10 (0.91, 1.32)	0.3
	Q3	1.22 (1.04, 1.44)	0.018	1.14 (0.96, 1.35)	0.12	1.06 (0.89, 1.27)	0.5
	Q4	1.77 (1.46, 2.14)	< 0.001	1.66 (1.34, 2.05)	< 0.001	1.40 (1.11, 1.76)	0.005
Short sleep duration	ZJU (continuity)	1.23 (1.13, 1.32)	< 0.001	1.20 (1.10, 1.30)	< 0.001	1.17 (1.08, 1.27)	< 0.001
	ZJU (categorical)						
	Q1	Reference		Reference		Reference	
	Q2	1.26 (1.07, 1.49)	0.007	1.32 (1.11, 1.58)	0.003	1.35 (1.13, 1.62)	0.002
	Q3	1.27 (1.05, 1.53)	0.013	1.32 (1.09, 1.60)	0.006	1.32 (1.09, 1.61)	0.007
	Q4	1.62 1.37, 1.91)	< 0.001	1.56 (1.31, 1.86)	< 0.001	1.51(1.25, 1.83)	< 0.001
Long sleep duration	ZJU (continuity)	1.01 (0.81, 1.26)	> 0.9	0.94 (0.74, 1.18)	0.6	0.91 (0.71, 1.18)	0.05
	ZJU (categorical)						
	Q1	Reference		Reference		Reference	
	Q2	0.61 (0.39, 0.96)	0.034	0.56 (0.35, 0.89)	0.015	0.57 (0.35, 0.97)	0.021
	Q3	0.56 (0.34, 0.91)	0.021	0.47 (0.29, 0.78)	0.004	0.46 (0.27, 0.79)	0.006
	Q4	0.86 (0.59, 1.25)	0.4	0.72 (0.48, 1.07)	0.010	0.66 (0.40, 1.09)	0.010

Note. CI, confidence interval; OR, Odds ratio; Q, Quartiles; ZJU, ZJU index.

Model 1: No covariates adjusted;

Model 2: Adjusted for Age, HbA1c, Race, Education, Marital, PIR;

Model 3: Adjusted for Age, HbA1c, Race, Education, Marital, PIR, Smoke, Drink, Work Activity, Physical Activity, Hyperlipidemia, Hypertension, CVD, Depression.

3.3 Nonlinear Association between the ZJU Index and Sleep-related Problems

Multivariate adjusted RCS analysis revealed a U-shaped nonlinear association between the ZJU index and sleep disorders (*P*-nonlinear = 0.0001), with an inflection point at 37.7. There was no non-linear relationship between the ZJU index, self-reported difficulty falling asleep (*P*-nonlinear = 0.060), and short sleep duration (*P*-nonlinear = 0.3502) (Figure 2).

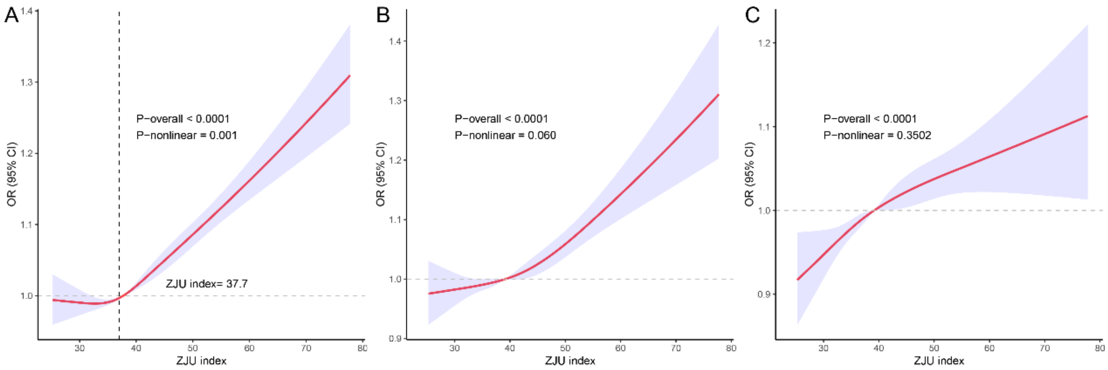

Figure 2. RCS Curve Fits the Association of the ZJU Index with Three Types of Sleep-related Problems

Note. Figure 2A. RCS curve depicting the relationship between the ZJU Index and sleep disorders; Figure 2B. RCS curve depicting the relationship between the ZJU index and self-reported difficulty falling asleep; Figure 2C. RCS curve depicting the relationship between the ZJU index and short sleep duration. Adjusted for Age, HbA1c, Race, Education, Marital, PIR, Smoke, Drink, Work Activity, Physical Activity, Hyperlipidemia, Hypertension, CVD, Depression.

3.4 Subgroup Analysis

Subgroup analysis was used to show the differences between the ZJU index and sleep-related problems in some subgroups. Figure 3 shows differences mainly in terms of age, PIR, education, hypertension and depression. The full forest plot is presented in the supplementary material (Figure S1-S4).

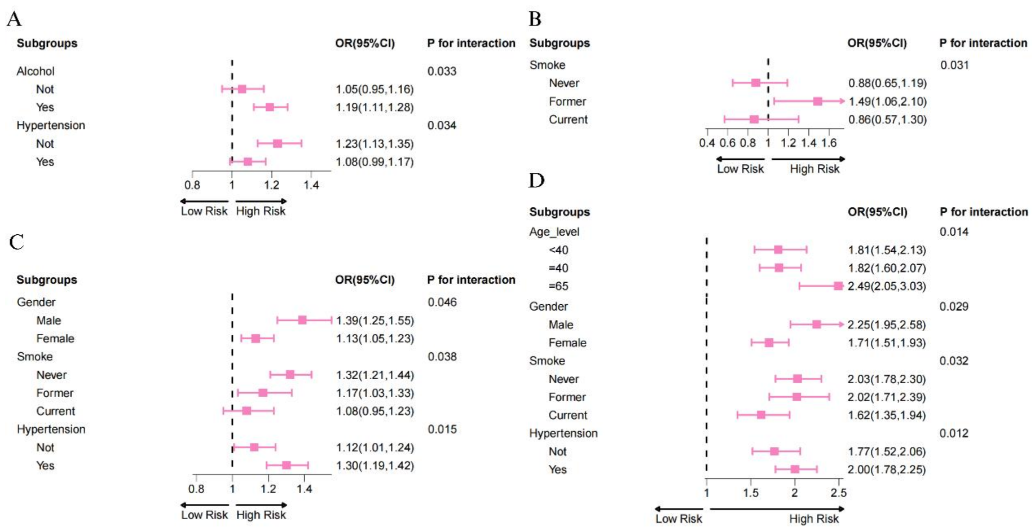

Figure 3. Part Subgroup Analysis of the Association of the ZJU Index and the Risk of Sleep-related Problems

Note. Figure 3A. The forest diagram group analysis of all individuals with short sleep duration; Figure 3B. The forest diagram group analysis of all individuals with sleep disorders. Each stratification was adjusted for Age, HbA1c, Race, Education, Marital, PIR, Smoke, Drink, Work Activity, Physical Activity, Hyperlipidemia, Hypertension, CVD, Depression. CI, confidence interval; PIR, poverty income ratio; OR, odds ratio.

3.5 Predictive Value of the ZJU Index for Sleep-related Problems

A univariate logistic regression model was used to evaluate the predictive power of the ZJU index for sleep-related problems across different age groups and genders and to compare its performance with other individual lipid measures. As shown in Figure 4, the ZJU index demonstrated a high predictive value (AUC = 0.710) for elderly women who were diagnosed with sleep disorders by their healthcare providers. When compared TG, TC, LDL, and HDL, the ZJU index outperformed these measures in predicting sleep-related problems, suggesting that this new indicator has greater validity in early prediction of sleep problems.

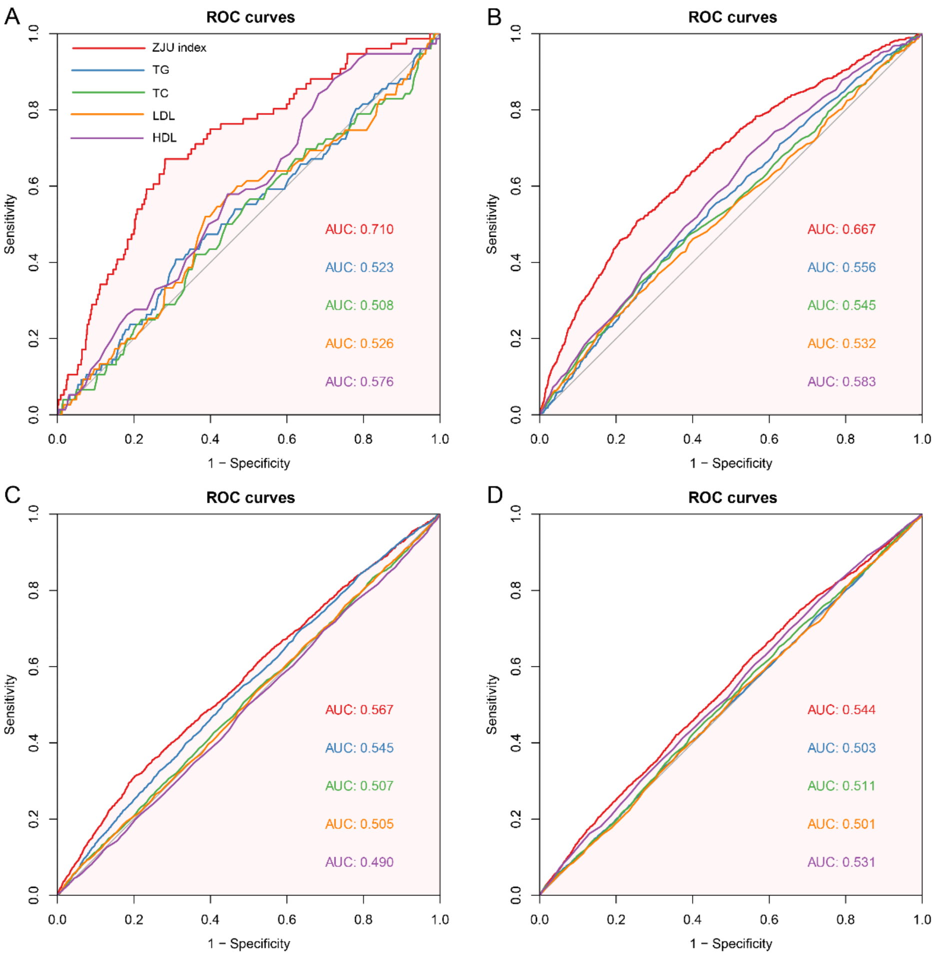

Figure 4. Comparison of ROC Curve for the ZJU Index, Single Indicators and Lipid Metabolism Indicators to Sleep-related Problems

Note. Figure 4A. ROC curve in elderly females with sleep disorders; Figure 4B. ROC curve in all individuals with sleep disorders; Figure 4C. ROC curve in all individuals with self-reported difficulty falling asleep; Figure 4D. ROC curve in all individuals with short sleep duration. AUC: area under the curve; FPG: fasting plasma glucose; HDL: high-density lipoprotein; ROC: receiver operating characteristic; TG: triglycerides; TC: total cholesterol; ZJU index: Zhejiang University index.

4. Discussion

In this study, the basic data of enrolled participants with sleep-related problems had significant statistical differences in gender, race, income factors, lifestyle habits, and chronic diseases. The ZJU index for individuals with sleep-related problems is generally higher compared to those without such problems. This statistical evidence highlights a significant disparity in the ZJU index between populations with sleep-related problems and those without, suggesting a strong correlation between metabolic disorders and the incidence of sleep-related problems. With further analysis of the association of the ZJU index and all types of sleep disorders, it can be inferred that an elevated the ZJU index is associated with diminished metabolic capability and an increased risk of sleep disorders. It is worth noting that people with over 39 scores of the ZJU index have a higher risk of insufficient sleep duration as they have already suffered metabolic disorders, which is proved by the RCS models. Further ROC curve analysis by adjusting for age and gender revealed that the ZJU index had a high predictive value in elderly women who reported hospital diagnoses of sleep disorders. As a composite indicator, the ZJU index proved to be more effective than single lipid indicators in predicting the happen of sleep-related problems, especially in individuals with a confirmed diagnosis of sleep disorders.

The ZJU index comprises indicators pertaining to liver enzymes, glucose metabolism, and lipid metabolism, and was initially employed as a predictive indicator for NAFLD [12]. The liver is a key hub for many physiological processes in the human body, responsible for glucose metabolism, lipid metabolism, and cholesterol metabolism, and is closely related to the body's metabolic level [21]. Impaired liver function can lead to dysregulation of blood sugar and lipid levels, indirectly causing sleep-related problems. Glucose metabolism and lipid metabolism affect sleep quality at different levels, and their roles will be further discussed in the following text.

The ZJU index reflects human metabolic status, suggesting that diabetes and obesity may play a role in the development of sleep disorders. There exists a bidirectional relationship between blood sugar and sleep-related problems, which effectively creates a vicious cycle. On the one hand, individuals with type 2 diabetes and related comorbidities, such as obesity, nocturnal hypoglycemia, increased sympathetic nerve activity, neuropathic pain caused by peripheral nerve injury, and nocturia, may become one of the reasons for having sleep disorders [22]. Furthermore, scientists have found that slow-wave sleep duration is reduced in diabetic patients, suggesting that this difference in sleeping structure may affect blood sugar levels and then have a negative effect on sleep quality ulteriorly [23,24]. On the other hand, some of the recommended treatments for sleep disorders show potential positive effects on type 2 diabetes and even other metabolic diseases [9]. The American Diabetes Association has highlighted that the control of blood sugar levels could be promoted by improving sleep in those suffering type 2 diabetes. Thus the improvement of sleep quality helps prevent the progression of type 2 diabetes, thereby enhancing overall quality of life [25]. Cizza et al. reported that by increasing sleep duration with an average time of 31 minutes, a greater glucose metabolism occurs, with a decrease of FPG by 9mg/dL fasting insulin decrease of 4IU/mL, and an increase of Quiki index by 7% [26]. Besides, Suvorexant, an orexin receptor antagonist, significantly improved the sleep quality of diabetic patients and obesity-related parameters within 14 weeks [27]. In another study, better sleep quality and lower FPG could be observed in type 2 diabetes and insomnia patients with treatment of dextrolindone for 14 days [28]. Epidemiological data indicated that reduced sleep duration is associated with changes in lipid profiles and various other metabolic diseases [29]. A study based on the Finnish population found that two genetic variants, which are respectively related to lipid metabolism and sleep duration, are located on the same chromosome near gene *TRIB1* thus it could be conjectured that lipid metabolism and sleep duration may have genetic correlation [30]. Both NHANES and the China Health and Nutrition Survey have reported that a stronger connection between lipids and sleep appears in the female population [31,32]. However, Existing epidemiological studies on the association between sleep duration and lipid metabolism disorders are controversial [31,33,34]. Therefore, relying solely on a single metabolic index may not be sufficient to screen people with sleep-related problems, which is consistent with our findings.

This article further illustrates that the ZJU index possesses significant predictive value for sleep disorders in elderly women, which is related to metabolic disorders in elderly women. Sleep disturbances are common in elderly women, affecting over 40% to 60% of perimenopausal or postmenopausal women [35]. Perimenopause stage may exacerbate the risk of sleep disorders [36]. Postmenopausal women with high BMI and abdominal obesity are more likely to have the root cause of sleep disorders, with reduced deep sleep quality and sleep efficiency [37]. Therefore, focusing on metabolic disorders and sleep problems in elderly women may be one of the future research directions. Early intervention to ameliorate metabolic disorders in this demographic may serve as a preventive measure against the onset of sleep-related problems.

In existing studies, the ZJU index is mainly used to evaluate and predict related diseases in the Chinese population, while this study includes data from US adults in order to test its wide applicability in the population. This study classified sleep-related problems and explored the comprehensive metabolic levels of people with different sleep problems. Among them, the ZJU index has a higher predictive value in elderly women and can be used as an important indicator to assess the risk of sleep disorders in this population. However, this study has certain limitations. Due to the lack of intervention measures, the temporal and causal relationship between sleep-related problems and the body's metabolic level cannot be explored. Data are collected from personal recollections and self-reports, which may be biased. Therefore, the association between sleep-related problems and the body's comprehensive metabolic level requires stronger evidence in the future.

5. Conclusion

The ZJU index is significantly correlated with sleep problems in US adults. Notably, as the ZJU index increases, the risk of sleep-related problems increases. Consequently, monitoring elevated ZJU index levels is beneficial for the early detection and management of sleep disorders within the population, particularly among elderly women.

Declarations

Ethics approval and consent to participate

Data collection for the NHANES was approved by the NCHS Research Ethics Review Board. An individual investigator utilizing the publicly available NHANES data do not need to file the institution internal review board.

Consent for publication

Not applicable

Data Availability

The dataset analyzed in the current study is available from the NHANES repository [https://www.cdc.gov/nchs/nhanes/].

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Appendix

ALT: alanine aminotransferase;

AST: aspartate aminotransferase;

AUC: area under the curve;

BMI: body mass index;

CI: confidence interval;

CVD: cardiovascular disease;

FPG: fasting plasma glucose;

HbA1c: glycosylated hemoglobin

HDL: high-density lipoprotein;

IQR: interquartile range

NAFLD: non-alcoholic fatty liver disease;

NHANES: National Health and Nutrition Examination Survey;

OR: odds ratio;

ORs: odds ratios;

PIR: poverty income ratio;

RCS: restricted cubic spline;

ROC: receiver operating characteristic

TC: total cholesterol;

TG: triglycerides;

ZJU index: Zhejiang University index